

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

I. AMENDMENTS

In the Claims:

Please cancel, without prejudice or disclaimer, claims 35 to 46. Please amend claims 47, 48 and 55 to 59, as shown below by deleting the stricken-through material and inserting the underlined material as follows:

35. (Currently Canceled) ~~A method for the treatment of a cancer in a subject, the method comprising:~~

- ~~(a) determining a genomic polymorphism in the subject with said cancer;~~
 - ~~(b) selecting a chemotherapeutic drug to administer to said subject to treat said cancer depending on the type of genomic polymorphism determined in step (a); and~~
 - ~~(c) administering said chemotherapeutic drug to said subject,~~
- ~~wherein the cancer is a cancer selected from the group consisting of breast cancer, colorectal cancer, gastric cancer, esophageal cancer, Burkitt's lymphoma, B follicular cell lymphoma and small cell lung carcinoma.~~

36. (Currently Canceled) ~~The method of claim 35 wherein the cancer is colorectal cancer.~~

37. (Currently Canceled) ~~The method of claim 35 wherein determining the genomic polymorphism of the subject comprises determining the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidylate synthase (TS) gene's 5' untranslated region (UTR), wherein the genotype is homozygous for a triple repeat of the tandemly repeated sequence, heterozygous for a double repeat and a triple repeat of the tandemly repeated sequence, or homozygous for a double repeat of the tandemly repeated sequence.~~

38. (Currently Canceled) ~~The method of claim 36 wherein the chemotherapeutic drug is a TS-directed drug.~~

39. (Currently Canceled) ~~The method of claim 37 wherein the TS directed drug is a fluoropyrimidine.~~

40. (Currently Canceled) ~~The method of claim 38 wherein the fluoropyrimidine is 5-fluorouracil.~~

41. (Currently Canceled) ~~The method of claim 39 wherein the subject is a human subject.~~

42. (Currently Canceled) ~~The method of claim 40 wherein determining the subject's genotype further comprises:~~
~~extracting genomic DNA from a biological sample of the subject;~~
~~amplifying the 5' UTR of the thymidylate synthase gene of said genomic DNA using polymerase chain reaction; and~~
~~analyzing the polymerase chain reaction product to determine the subject's genotype.~~

43. (Currently Canceled) ~~The method of claim 44 wherein analysis of the polymerase chain reaction product is performed using electrophoresis.~~

44. (Currently Canceled) ~~A method for the treatment of a cancer in a subject, the method comprising:~~
~~(a) determining the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidylate synthase gene's 5' UTR, wherein the subject's genotype is homozygous for a triple repeat of the tandemly repeated sequence, heterozygous for a double repeat and a triple repeat of the tandemly repeated sequence, or homozygous for a double repeat of the tandemly repeated sequence, and~~
~~(b) administering a TS directed drug to the subject if the subject's genotype is homozygous for a double repeat of the tandemly repeated sequence;~~
~~wherein the cancer is a cancer selected from the group consisting of breast cancer, colorectal cancer, gastric cancer, esophageal cancer, Burkitt's lymphoma, B follicular cell lymphoma and small cell lung carcinoma.~~

45. (Currently Canceled) ~~The method of claim 43 wherein determining the subject's genotype further comprises:~~
~~extracting genomic DNA from a biological sample of the subject;~~
~~amplifying the 5' UTR of the thymidylate synthase gene of said genomic DNA using polymerase chain reaction; and~~
~~analyzing the polymerase chain reaction product to determine the subject's genotype.~~

46. (Currently Canceled) ~~The method of claim 44 wherein analysis of the polymerase chain reaction product is performed using electrophoresis.~~

Please amend the following claims:

47. (Currently Amended) A method for ~~determining the suitability of treating a cancer in a subject using a chemotherapeutic drug, the method~~ screening cancer cells for sensitivity to a chemotherapeutic drug, comprising:

taking a biological sample of said cancer cells from a ~~the~~ subject; and

~~using the biological sample to determine~~ determining the genotype of a pre-selected gene of the cancer cells ~~subject~~, wherein said genotype determines the intratumoral expression of said gene; ~~and correlating wherein said gene expression determines the response of the subject to said sensitivity to said~~ chemotherapeutic drug.

48. (Currently Amended) The method of claim 47 wherein ~~the~~ said cancer cells are is colorectal cancer cells.

49. (Currently Amended) The method of claim 48 wherein ~~the~~ said pre-selected gene is thymidylate synthase gene.

50. (Previously Added) The method of claim 49 wherein determining the genotype comprises determining the subject's genotype at a tandemly repeated 28 base pair sequence in the thymidylate synthase (TS) gene's 5' untranslated region (UTR), wherein the genotype is homozygous for a triple repeat of the tandemly repeated sequence, heterozygous for a double repeat and a triple repeat of the tandemly repeated sequence, or homozygous for a double repeat of the tandemly repeated sequence.

51. (Previously Added) The method of claim 50 wherein the chemotherapeutic drug is a TS directed drug.

52. (Previously Added) The method of claim 51 wherein the TS directed drug is a fluoropyrimidine.

53. (Previously Added) The method of claim 52 wherein the fluoropyrimidine is 5-fluorouracil.

54. (Previously Added) The method of claim 53 wherein the subject is a human subject.

55. (Currently Amended) The method of claim 54 wherein determining the subject's genotype ~~further~~ comprises:

~~extracting genomic DNA from a biological sample of the subject;~~

~~amplifying the~~ determining the genotype at the 5' UTR of the thymidylate synthase gene of
said genomic DNA from said cell using polymerase chain reaction; and

~~analyzing the polymerase chain reaction product to determine the subject's genotype.~~

56. (Currently Amended) The method of claim 55 wherein said determining the genotype is
by analysis of the polymerase chain reaction product of the 5'UTR is performed using
electrophoresis.

57. (Currently Amended) A kit for use in screening for the effectiveness of TS directed drug
therapy in human subjects, the kit comprising: means for determining a genomic polymorphism
of the 5' UTR of the TS gene; and instructions for correlating the genomic polymorphism of the
5' UTR of the TS gene to sensitivity to TS directed drug therapy use of the kit.

58. (Currently Amended) The kit of claim 57 wherein the means for determining said
genomic polymorphism ~~comprise:~~ all or some of the positive controls, negative controls,
reagents, primers, sequencing markers, and probes for determining the presence or absence of a
tandemly repeated 28 base-pair nucleic acid sequence that defines the genomic polymorphism in
the 5' UTR of the TS gene ~~gen~~.

59. (Currently Amended) The kit of claim 58 wherein the kit components may be provided
in solution or as a liquid dispersion ~~or the like~~.

60. (Previously Added) The kit of claim 58 comprising DNA tandemly repeated sequences
that determine the type of genomic polymorphism of the TS gene in Tris-EDTA buffer solution
kept at about 4°C.